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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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James Leushner

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EXAMINER

WILDER, CYNTHIA B

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

11/09/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/802,110

Applicant(s)

LEUSHNER ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-16, 18-25 and 27-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-16, 18-25 and 27-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/20/2007 has been entered. Claims 1-13, 17 and 26 have been canceled. Claim 14 has been amended. Claims 14-16, 18-25 and 27-36 are pending in the instant invention.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Previous Rejections

2. The prior art rejections under 35 USC 103(a) are withdrawn in view of the new grounds of rejections necessitated by Applicant's amendment of the claims.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENTS OF THE CLAIMS:

Claim Objections

3. Claims 18-20 are objected to because of the following informalities: The claims 18-20 are objected because they all depend from the claim 17 which is canceled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 18 and 20 are indefinite because they are redundant to the claim 14 and does not further limit the independent claim 14 as currently amended.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 14-16, 18-25 and 27-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Digby et al and Ruano in view of Rao (see citation in prior Office actions). Regarding claims 14-16, 18-21, 23-25, 27-28, 30-33, and 35-36, Digby et al

teach a kit for sequencing a specific region from a gene, said kit consisting of, in package combination at least one reaction vessel or a plurality of reaction vessels for each of the regions to be sequenced containing a mixture of a plurality of sequencing primers, one for each gene region to be evaluated. The plurality of sequencing primers each comprising a reactive portion which specifically hybridizes with the DNA in the sample and a label portion, the label portions of the primers being different and distinguishable one from the other (col. 7, lines 11-20). Digby et al further teach wherein kit may further comprise a thermally stable polymerase enzyme, deoxynucleotide triphosphate feedstock, dideoxynucleotide triphosphate and buffer (col. 3, lines 1-9 and col. 6, lines 58-60). Digby et al teach that the kit and method are useful for evaluating a desired target sequence in a plurality of sample (col. 1, lines 47-54).

Digby et al do not expressly teach wherein a primer specifically binds to the sense strand of said DNA region and a primer specifically binds to the antisense strand of said DNA region and wherein said primers flank one of the DNA regions with the genomic DNA. Digby et al do not expressly teach wherein the dideoxynucleotide triphosphate is present in a mole ratio to the corresponding deoxynucleotide triphosphate of from 1:50 to 1:1000 or 1:100 to 1:500.

Ruano et al. teach a mixture and method for sequencing genomic DNA sample, the method comprising amplifying in vitro with two locus specific primers that flank both ends of the target region to obtain a template, synthesizing simultaneously truncated strands from both ends of the template by introducing a dideoxynucleotide terminator for each of the four bases adenine, guanine, cytosine and thymine and introducing a label

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or labels specific for either or both of the 5' ends of the synthesizing strands, thermally cycling steps to provide a sufficiently readable signal (col. 2, lines 3-23, See Figure 5). Ruano et al teach wherein one of said specific primers specifically binds to the sense strand and the other primer specifically binds to the antisense strand (col. 12, lines 50-61). Ruano further teaches wherein the dideoxynucleotide triphosphate is in a mole ratio of about 1:10 to the corresponding deoxynucleotide triphosphate (col. 6, lines 47-68).

The reference of Ruano differs from the instant invention in that the reference does not teach wherein the method comprises the dideoxynucleotide triphosphate in a mole ratio of 1:50 to 1: 1000 or in a mole ratio of 1:1000 to 1:500 to the corresponding deoxynucleotide triphosphates.

In a method similar to that of Ruano, Rao teaches a method of direct sequencing of polymerase chain reaction-amplified DNA. Rao teaches wherein the method comprises mixing the PCR-amplified genomic DNA, labeled primer sequencing buffer and Taq polymerase in a tube, adding to the mixture in four separate tubes, four dNTPs and at least one dideoxynucleotide triphosphate, perform thermal cycling (see Table 3, page 5). Rao differs from the instant invention in that Rao does not teach wherein the mole ratio of the ddNTP:dNTP is from 1:50 to 1:1000 or 1:100 to 1:500. Rao also does not teach wherein the polymerase enzyme incorporates dNTPs into an extending nucleic acid polymerase at a rate which is no less than 0.5 times the rate of incorporation of dNTPs. However, Rao discloses that the composition of the dNTP/ddNTP mix varies depending on the type of polymerase preparation used. Rao states that different polymerases require different dNTP/ddNTP ratios for optimal chain

terminations and therefore, the reagents or kits for one polymerase cannot be substituted with those for a different polymerase. Rao further teaches that optimal buffer conditions for the synthesizing reaction will vary based on the specific DNA polymerase used (see Table 3 legend).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to provide primers which specifically binds to the sense strand of a DNA region and primers which specifically binds to the antisense strand of a DNA region, wherein said primers flank the desired DNA region in a mixture and kit as taught by Digby et al for the benefit of coupling genomic amplification with a process of DNA sequencing via dideoxynucleotide chain termination (col. 1, lines 17-23) as taught by Ruano et al. It would have further been *prima facie* obvious to one of ordinary skill in the art at the time of the claim invention that the mole ratio of ddNTP to dNTP in the kit of Digby would vary depending on the specific polymerase utilized as taught by Rao. Additionally, both Digby and Rao teach wherein the polymerase used is THERMOSEQUENASE, which is the same enzyme as used by Applicant. Therefore, the limitation extending nucleic acid polymer at a rate, which is no less than 0.4 times the rate of incorporation of deoxynucleotides, is an inherent property of the polymerase enzyme, THERMOSEQUENASE.

Regarding claims 22, 29 and 34, Digby et al teach the kit of claim 14, wherein the kit includes four-deoxynucleotide triphosphate and at least one dideoxynucleotide triphosphate (col. 3, lines 1-9).

Applicant's Traversal and Examiner's Response

(9) In response to Applicant's remarks and comments concerning the relationship of the instant invention to prior applications, the Examiner acknowledges Applicant's remarks, but notes that patentability of an application is determined on a case by case basis and each application is examined on its own merits. The instant invention is drawn to a kit, which is a product comprising reagents for a desired process. A kit cannot perform any method steps, but only contain reagents that can be used by a practitioner for a desired process. Thus, such arguments concerning the advantages of the instant kit are intended uses, which does not carry any patentable weight. In regards to Applicant's remarks concerning the relationship of the instant invention to that of US patent 6214555, Applicant is again reminded that each application is examined on its own merits. The examiner acknowledges the terminal disclaimers filed in the instant application and therefore no double patenting issues are currently discussed.

Conclusion

10. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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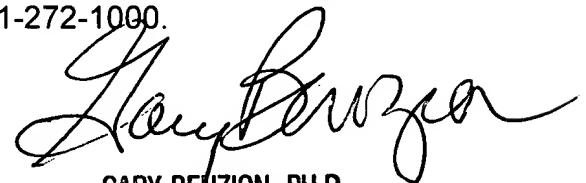
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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